REMARKS

This amendment is filed in response to an office action mailed September 2,2004, in which the Examiner rejected claims 1-3, 5, 15-30, 60-63, and 67-70 under 35 U.S.C. §103 as obvious over U.S. Patent serial number 6,348,583 ("Segev") in light of U.S. Patent serial number 5,512,462 ("Cheng").

The present amendment (1) adds new claims 71 through 74, (2) addresses the issue of whether motivation existed to combine Segev with Cheng, and (3) addresses issues relating to individual claims.

New claims 71 through 74 do not add any new matter. Claim 71 combines limitations found in previously presented claims 22 and 26 through 28. Claim 72 combines limitations found in previously presented claims 19 and 24. Claim 73 is identical to claim 25, except that the group from which the DNA polymerase is selected is smaller. Claim 74 is identical to claim 30, except that the group from which the polymerase enzyme is selected is smaller. Claims 71 through 74 are all drawn to the same invention as previously pending claims 1-3, 5, 15-30, 60-63, and 67-70.

In paragraph 6, the Examiner rejected claims 1-3, 15-18, 20-30, 60-63, and 67-70 as obvious over Segev in light of Cheng. Segev taught the use of certain compounds in connection with nucleotide mimetics. Cheng taught certain methods relating to PCR amplification; however, Cheng did not disclose the inventive compounds. According to the Examiner,

> Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have modified and improved the use of the adjuvant or cosolvent of Segev with the inclusion of Segev with the inclusion of PCR components of Cheng in order to achieve a sensitive and enhanced PCR composition as a whole. An ordinary practitioner would have been motivated to add the PCR

> components because Cheng taught that use of cosolvents influence the efficiency of amplification of the template by increasing the thermal stability of the DNA polymerase and reduces the loss of DNA polymerase activity during repeated high-temperature denaturation steps (see column 9, lines 20.-7). Therefore, an ordinary artisan would have been clearly motivated to have modified the compound taught by Segev with the addition of PCR components to achieve efficient and improved PCR system.

While Cheng does teach the use of cosolvents to influence amplification, among many other factors, Cheng does not mention the inventive compounds. On the contrary, he mentions other specific compounds, such as glycerol and DMSO. Nor does Cheng provide any factors by which compounds preferable to glycerol and DMSO can be identified. Indeed, Cheng does not even address the issue of whether solvents more efficacious than glycerol and DMSO might exist.

While Segev discloses certain general properties of PNA-DNA hybrids (col. 27, lines 5-35), Segev does not disclose any factors that would lead one to believe that use of the inventive compounds in the present application *in lieu of some other cosolvent* would increase the thermal stability of the DNA polymerase or reduce the loss of DNA polymerase activity during repeated high-temperature denaturation steps. It is impermissible hindsight to assume that one of ordinary skill in the art would have selected the inventive compounds of the present application to combine with Cheng even if Segev disclosed some of them. In the absence of a reference providing adequate motivation, an obviousness rejection is improper. "The mere fact that references <u>can</u> be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination." Manual of Patent Examining Procedure §2143.01 (citation omitted).

Moreover, the inventors, in the specification, identified factors affecting the desirability of various compounds for use in, for example, PCR amplification reactions. For example, on pages 11 and 12 of the specification, the inventors discuss the ring structure of the inventive compounds and the interaction of such compounds with GC rich templates. The inventors also identified criteria by which additives could be evaluated: potency, specificity, and effective range (specification, page 9). Finally, the inventors through experimental studies identified particularly advantageous addititives and validated their theoretical insights. (Specification pages 36-42.) Because the Examiner did not cite any reference teaching why the inventive compounds possessed properties particularly desirable for use as solvents in PCR amplification reactions, because Cheng did not teach any factors for use in selecting solvents, and because glycerol and DMSO were adequate solvents for use in accordance with Cheng's invention, it cannot be assumed that Cheng would have utilized such compounds had he been aware of their existence (but unaware of the inventors' research). The mere fact that one of a great number of solvents exists is not a sufficient reason to utilize it absent some motivation, such as a theoretical insight.

Thus, one of ordinary skill in the art would have no motivation to combine the teachings of Cheng with those of Segev. The applicant therefore believes that all of the outstanding claims of the present application are allowable over Segev in light of Cheng.

With respect to claim 26, the Examiner does not identify any teaching suggesting or disclosing the limitation "wherein the reaction adjuvant has a potency of at least 75% of the potency of DMSO or formamide in an equivalent polynucleotide chain reaction (PCR)".

With respect to claim 27, the Examiner does not identify any teaching suggesting or disclosing the limitation "wherein the reaction adjuvant has a specificity of at least 80% of the specificity of DMSO or formamide in an equivalent polynucleotide chain reaction (PCR)".

With respect to claim 28, the Examiner does not identify any teaching suggesting or disclosing the limitation "wherein the reaction adjuvant has an effective range spanning at least 0.1 M".

With respect to claim 29, the Examiner does not identify any teaching suggesting or disclosing the limitation "wherein the polynucleotide template comprises greater than 50% G+C".

With respect to claim 71, the Examiner does not identify any teaching suggesting or disclosing the limitations "wherein the reaction adjuvant has a potency of at least 75% of the potency of DMSO or formamide in an equivalent polynucleotide chain reaction (PCR)", "wherein the reaction adjuvant has a specificity of at least 80% of the specificity of DMSO or formamide in an equivalent polynucleotide chain reaction (PCR)", and "wherein the reaction adjuvant has an effective range spanning at least 0.1 M".

With respect to claim 73, the Examiner does not identify any teaching suggesting or disclosing the limitation "wherein the one or more polymerases or fragments thereof is selected from the group consisting of Taq polymerase, Tme polymerase, Pfu Polymerase, DNA polymerase I, Klenow fragment and reverse transcriptase".

With respect to claim 74, the Examiner does not identify any teaching suggesting or disclosing the limitation "wherein the one or more polymerase enzymes or fragments

thereof is selected from the group consisting of Taq polymerase, Tme polymerase, Pfu polymerase, DNA polymerase I, Klenow fragment and reverse transcriptase".

For the above reasons, the applicant believes that claims 1-3, 5, 15-30, 60-63, and 67-74 are allowable over the prior art of record and requests that a timely Notice of Allowance be issued.

Respectfully Submitted,

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